REMARKS

1. After filing the October 7, 2009, it came to Counsel's attention that there were two new claims numbered "190". To comply with 37 CFR 1.126, we have renumbered the second "190" claim as 191, and claims "191"-"218" as 192-219, adjusting dependencies as needed. Note that this correction also affects the discussion of claims on pp. 52-55 of the main amendment.

2. We have deleted an extra comma from claim 1, corrected a spelling error in claim 100, and amended the claim presented as "195" but now renumbered as "196" to label the five components of the R1 Markush group as (a)-(e). Claim 212 (as renumbered) now parallels 191 (as renumbered).

3. We wish to call to the examiner's attention the disclosure of Porcelli, WO2008/133801, which demonstrates that additional compounds within the scope of the claim are indeed active and therefore operative[1]. While this is postfiling evidence, it is being used to establish that in fact these compounds are immunologically active and hence <u>can</u> be used as the present specification taught they could be used, i.e., for immunomodulation.

Compounds DB03-4, DB03-05, DB03-10, DB04-9 and DB03-06, which all showed <u>in vitro</u> cytokine-modulatory activity (Porcelli P35, L3-6), all fall within the polyunsaturated moiety subgenus (claim 7) of the present claims. In particular, R3 is of the form set forth in claim 177, i.e.,

$-C(=O)(CH_2)_k(CH=CHCH_2)_2(CH=CHCH_2)_n(CH_2)_mCH_3$.

Likewise A is of the form specified in (as renumbered) claim 196, wherein A is CHOH-R1.

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[1] Some of the data was previously disclosed in Porcelli, WO2006/026389.

Comparing compound **5** of Fig. 11 with the Porcelli compounds, we have (Table A):

Compound	R3/claim 177			A/claim 195		R
	k	n	m	R1formula	i	
Fig. 11, **5**	3	2	3	(b)	12	α-D-Gal
DB03-4	9	0	3	(c)	13	α-D-Gal
DB03-5	3	2	3	(c)	13	α-D-Gal
DB03-10	7	2	3	(c)	13	α-D-Gal
DB04-9	8	2	3	(c)	13	β-D-Man
DB03-6	3	3	1	(c)	13	α-D-Gal

Studying the above table, it is apparent that in R3, one can vary the number of double bonds, as well as the spacing between the -C(=O)- and the first double bond. Likewise, it is clear that the double bond in A is not required for activity. Finally, DB04-9 evidences that it is not necessary that R be galactose.

Porcelli also prepared GalCer analogues with polyunsaturated moieties of the conjugated type, see his DB05-9, DB05-10, DB05-11, DB05-12, DB05-14, DB05-15, DB05-16 and DB05-17 on pp. 37-38. We disclose conjugated systems at P70, L23-31.

Fig. 12 shows that all of these compounds stimulate IFN-gamma production to some degree with DB05-12 being the best. Fig. 13 shows that they all stimulate IL-4 production, and indeed all were superior in this regard to DB04-1. Fig. 14 shows that all save perhaps DB05-17 stimulate (D1d-dependent proliferation. See also Figs. 15-16.

4. We have added new claims 220-230 which parallel claim 177 but are dependent on 171, 189, or as renumbered, 191, 193, 194, 196, 197, 201, 210, 212 or 213, respectively. Since

claims 206-209 (as renumbered) inadvertently duplicated claims 202-205 (as renumbered), we added new claim 231 which is like 196 (as renumbered) but dependent on 171, and made 206 dependent on 231.

5. We compare the scope of selected claims below (Table B):

Table B: Comparison of Selected Dependent Claims					
Selected Claim	R	Ch	R2	R3	A
3		O			
4			H		
7				comprises PUM	
148	compr CHO	O			
149	compr Gal	O			
153		O	H		
154				-C(=O)-PUM	
158	Gal	O		R3 of **5**	A of **5**
159	compr CHO				
160	CHO				
92	",monosacch				
95	",list of sugars				
96	",inner is Gal				
167	1-5 from list; inner Gal or Glu				
168	from glycosylcer				

169	like 167	O	H		
170	like 168	O	H		
171	Gal	O	H		
172	like 167	O	H	-C(O)PUM, PUM is HC	
177	like 167	O	H	k/m/n formula for R3	
183	Gal	O	H	-C(O)PUM, PUM is HC	
187	like 167	O	H		CH_2OH, CHOH alkanyl or hydroxyalkanyl, or CHOH alkenyl or hydroxy alkenyl
189	like 167	O	H		CHOH alkanyl or hydroxyalkanyl, or CHOH alkenyl or hydroxy alkenyl
191	like 167	O	H		-CHOH-alkenyl or hydroxy alkenyl
*196	like 167	O	H	-	CHOH-R1 with five R1 formulae (a)-(e)
*197	Gal	O	H	like 183	like 187
*199	Gal	O	H		like 187
*201	Gal	O	H	-	like 189
*202	like 167	O	H	-C(O)PUM, PUM is HC	like 189
*203	like 167	O	H	"with size limit	like 189
*206	like 167	O	H	like 202	like 189

*207	like 167	O	H	like 203	like 189
*210	Gal	O	H	-	"with size limit
*212	Gal	O	H		CHOH -alkenyl or hydroxy alkenyl with size limit
*215	Gal	O	H	-C(O)PUM, PUM is HC	like 212
*216	Gal	O	H	"adds size limit	like 212
220	Gal	O	H	like 177	
221	like 167	O	H	like 177	like 189
222	like 167	O	H	like 177	like 191
223	like 167	O	H	like 177	-CHOH-CH=CH-alkanyl
224	like 167	O	H	like 177	CHOH-CH=CH-C_{7-21} alkyl
225	like 167	O	H	like 177	like 196
226	Gal	O	H	like 177	like 197
227	Gal	O	H	like 177	like 201
228	Gal	O	H	like 177	like 210
229	Gal	O	H	like 177	like 212
230	Gal	O	H	like 177	like 212 but single olefinic bond
231	Gal	O	H	-	like 196

*claim as renumbered, compr = comprises, CHO = carbohydrate, HC = hydrocarbon, PUM = polyunsaturated moiety, Gal = Galactose

6. Entry of this supplemental reply is proper because it corrects the numbering of the claims and presents new evidence in support of patentability, and because it was filed shortly after the main reply and therefore did not interfere with the preparation of the action on the main reply.

Respectfully submitted,

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Enclosure
-Porcelli, WO2008/133801 (cover page, pp. 20-22, 34-39, 48-54, Figs. 5A, 5C, 5D, 6-16)

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